REMARKS/ARGUMENTS

The claims are 3, 6-9 and 13-19. Claims 1, 2 and 10-12 have been canceled in favor of new claims 13, 14 and 17-19 respectively. Accordingly, claims 3 and 6-7, which previously depended on claim 1, have been amended to depend on new claim 13. These claims and claims 8 and 9 have also been amended to improve their form. In addition, claims 4 and 5 have been canceled, and new claims 15 and 16 have been added containing subject matter previously appearing in claims 6 and 8, respectively. Support for the claims may be found, *inter alia*, in the original claims. Reconsideration is expressly requested.

Claims 1-12 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-13 of co-pending application Serial No. 11/117,671. In response, Applicants are submitting herewith a terminal disclaimer and a certification of assignee signed by the managers of the assignee Polymerics GmbH, thereby overcoming the double-patenting rejection.

Claims 6 and 8-12 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the reasons set forth on page

3 of the Office Action. In response, Applicants have amended claims 6, 8 and 9 and have canceled claims 10-12 in favor of new claims 17-19 to improve the form of these claims, which it is respectfully submitted overcomes the Examiner's rejection under 35 U.S.C. §112, second paragraph.

Claims 1, 6 and 10-12 were rejected under 35 U.S.C. 102(b) as being anticipated by *Abe et al. U.S. Patent No. 4,202,775* which was cited in the International Search Report. The remaining claims were rejected under 35 U.S.C. 103(a) as being unpatentable over *Abe et al.* alone (claims 2-4) or further in view of *Davankov et al. U.S. Patent Application Publication No. 2003/0027879* (claims 5 and 7-9).

Essentially, the Examiner's position is that *Abe et al.* discloses the adsorbent material, method and use recited in the claims except for the specific vinylimidazole employed, the relative amounts of divinylbenzene and ethylvinylbenzene employed, and the specific surface of the adsorbent material, which are said to be within the skill of the art, and except for the manner in which the adsorbent material is prepared, which is said to be taught by *Davankov et al.*

This rejection is respectfully traversed.

As set forth in new claim 13, Applicants' invention provides an adsorbent material based on crosslinked, porous imidazole-divinylbenzene copolymers for application in blood-, blood plasma-, and albumin purification processes. The adsorbent material is formed by radical suspension polymerization of a monomer mixture of divinylbenzene crosslinker and an imidazole derivative. The polymerization is conducted in the presence of air and/or oxygen, a salt, a stabilizer, and an inert substance. The adsorbent material contains 5 weight % to 30 weight % of the imidazole derivative, has a specific surface from 200 m^2/g to 900 m^2/g and a total pore volume from 1.0 cm^3/g to 2.0 cm^3/g where 1 g of the material contains up to 0.3 cm^3 micropores, up to 1.2 cm^3 mesopores, and up to 0.5 cm^3 macropores, and is essentially of spherical shape having a particle size range from 1 µm to 300 µm.

As set forth in new claims 17-19, Applicants' invention provides a method of blood purification in which an absorbent material based on crosslinked, porous imidazole-divinylbenzene copolymers is provided. The adsorbent material is formed by specific radical suspension polymerization of a monomer mixture

in the presence of air and/or oxygen, a salt, and an inert substance. The adsorbent material includes at least 50 weight percent divinylbenzene crosslinker and 4 to 30 weight percent of an imidazole derivative. The absorbent material is highly crosslinked and highly porous, and has a spherical shape and specific characteristics of surface, pore size distribution, pore diameter, and particle size range, for application in blood-, blood plasma-, and albumin purification processes.

In accordance with claim 17, the adsorbent material is applied to blood or blood plasma. In accordance with claim 18, the adsorbent material is applied to blood in a Molecular Adsorbent Recirculating System (MARS). In accordance with claim 19, the adsorbent material is applied to blood as a sorbent for bilirubin and bile acids. In this way, Applicants' invention provides an essentially spherical body compatible with adsorbent material suitable for the removal of albumin-bound toxins, drugs, pharmaceuticals, endogenic and exogenic toxins from blood, blood plasma or albumin circuits, having high adsorption speed and capacity, and a method to produce this adsorbent material in a relatively simple and economical way.

The primary reference to *Abe et al.* discloses an adsorbent of porous copolymerizates, which is produced from a mono-ethylenically unsaturated monomer and a cross-linking monomer, and has pores with an average pore diameter (d) of 500 Å to 6000 Å, whereby the volume of the pores with an average diameter in the range of 0.5 d to 2 d is not more than 60% of the total pore volume of the pores in the copolymerizate. If the adsorbent according to *Abe et al.* is used for blood purification, it should first be pre-treated in such a manner that the plasma proteins are cross-linked after adsorption of the copolymerizate.

In contrast to *Abe et al.*, Applicants' invention is directed to a porous divinyl benzene imidazole copolymerizate, which surprisingly is suitable for blood purification only if the pores in the copolymer have average pore diameters in the range of 100 Å to 500 Å, and a specific pore size distribution, whereby up to 0.3 cm^3 micropores, up to 1.2 cm^3 mesopores, and up to 0.5 cm^3 macropores are contained in 1 g of the material, which means that the pores of the adsorbent according to claim 13 are present mainly in the micropore and mesopore range, which was classified as being **unsuitable** for blood purification methods in *Abe et al.* See column 7, lines 3-14 of *Abe et al.*, in which it is stated:

> "It is required for the present porous copolymer that the pores in the copolymer have an average pore diameter of from 500 Å to 6,000 Å, preferably 600 Å to 5,000 Å. If the average pore diameter is too small, the amount and rate of adsorption of organic compounds on the copolymer is reduced, and if the average diameter is too large, the strength of the copolymer is lowered and hence the copolymer is not adapted to practical use, and furthermore the surface of the copolymer is inevitably very small, resulting in a poor adsorbing capacity of the adsorbent."

These statements and the experimental proof provided for these statements in *Abe et al.* would lead one skilled in the art to conclude that removal of toxic compounds from blood proteins using porous imidazole divinyl benzene copolomers as recited in Applicants' claims was not possible. Applicants, however, overcame the prejudice of those skilled in the art that was expressed in *Abe et al.* to arrive at its adsorbent material and method as recited in new claims 13 and 17-19.

The defects and deficiencies of the primary reference to *Abe et al.* are nowhere remedied by the secondary reference to *Davankov et al.* *Davankov et al.* describes a polymeric adsorbent material with an enhanced portion of mesopores, which is formed in the presence of a porogen. The porogen is further specified as a solvent or a solvent mixture whose properties are chosen

such that they are close to a theta-solvent of the formed polymer.

It is important to remember that theta-solvents are always substance specific, i.e. they have to be selected specifically for a given polymer. Usually, theta-solvents are obtained by combination of a good solvent with a non-solvent. In most cases, a theta-solvent for one polymer is not a theta-solvent for another polymer. Therefore, a theta-solvent cannot be easily transferred to a polymer having a different composition. The solvents or mixtures of solvents mentioned by *Davankov et al.* are specifically selected for polystyrene. They are not theta-solvents for Applicants' divinylbenzene-vinylimidazole-copolymer as recited in the claims. Moreover, Applicants do not use theta-solvents to make the claimed adsorbent material.

Davankov et al. uses aromatic monovinyl compounds and aromatic divinyl compounds as monomers. These monomers are hydrophobic and non-polar. It has been known for a long time that for such hydrophobic, non-polar monomers and mixtures thereof the pore size can be controlled with the aid of mixtures of good solvents and non-solvents; however, it is respectfully submitted that this concept is not applicable to mixtures

containing a polar monomer because of the strong interactions of the polar monomer with other compounds of the mixture and because of the water solubility of the polar monomer.

In contrast, Applicants' imidazol monomers are strongly polar and hydrophilic, water soluble compounds to which the above-mentioned concepts for controlling the pore size cannot be applied. For this reason, Applicants could not use any teachings from *Davankov et al.* for controlling the pore size, but rather had to find their own solution for solving the problem presented by the prior art. Applicants would also like to point out that in fact, the inventors were unable to learn anything from *Davankov et al.* at the time of their invention because *Davankov et al.* was not published until February 6, 2003, and therefore was not known to the public at the time of the present application. Accordingly, it is beyond doubt that Applicants arrived at the invention without the knowledge of the *Davankov et al.*'s application. In any event, even if Applicants or anyone skilled in the art were aware of *Davankov et al.*, as stated above it is respectfully submitted that they would have no reason to use any teachings from *Davankov et al.* for controlling the pore size in view of *Davankov et al.'s* specific theta-solvents and hydrophobic and non-polar monomers.

For all these reasons, it is respectfully submitted that claims 13 and 17-19 are patentable over the cited references together with the dependent claims, which depend directly or indirectly on claim 13.

In summary, claims 3 and 6-9 have been amended, claims 1-2, 4-5 and 10-12 have been canceled, and new claims 13-19 have been added. A Terminal Disclaimer has also been submitted. A check in the amount of $100.00 is enclosed in payment of the fee for one additional independent claim over three for a small entity, and a check in the amount of $65.00 is enclosed in payment of the fee for the Terminal Disclaimer. In view of the foregoing, it is respectfully requested that the claims be allowed and that this case be passed to issue.

Respectfully submitted,
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